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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,494	11/27/2001	Susana Salceda	DEX-0293	1456

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	09/995,494	SALCEDA ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-9,15 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-9, 15 and 18-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response Applicants' response, filed on May 3, 2004. Claims 1-5, 7-9, 15 and 18-25 are pending and have been rejected herein. This action contains new rejections necessitated by Applicants' amendments. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-5, 7-9, 15 and 18-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-5, 7-9, 15 and 18-25 are indefinite over "prostate cancer specific" because it is not clear as to whether this nucleic acid (either RNA or DNA) is only found in prostate cancer samples, is expressed only in prostate cancer samples, or could be found or expressed in other samples, such as samples that are not prostate cancer samples (e.g., testes). In addition, since all cells would be expected to contain the DNA, it is not clear as to how the DNA can be considered to be "prostate cancer specific." It is also not clear if this recitation is only "prostate cancer specific" in humans or whether it can be specific in other animals as well. Furthermore, the specification does not specifically define this recitation.

B) Claims 1-5, 7-9, 15 and 18-25 are indefinite over "differentially expressed in prostate cancer tissue" because it is not clear as to what is meant or encompassed by this recitation. For example, it is not clear as to whether this means the claimed nucleic acid molecules were only expressed in prostate cancer tissue samples and not expressed in normal prostate tissue samples, or the claimed nucleic acid molecules were highly expressed in prostate cancer tissue samples, as compared to the expression in normal prostate tissue samples, etc. Furthermore, the specification does not define what is meant by "differentially expressed in prostate cancer tissue."

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-5, 7-9, 15 and 18-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility, or a well-established utility.

The pending claims have been reviewed in light of the Utility Examination Guidelines in the Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001, as well as the MPEP and existing law.

I. *The specification does not assert a substantial utility because the utilities asserted by Applicants requires or constitutes carrying out further research to identify or reasonably confirm a "real world" use.*

Applicants assert the claimed nucleic acid can be used in "methods for identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate." (see page 7, lines 15-18).

The specification teaches a data mining experiment for identifying nucleic acids (see pages 116-120). Specifically, the specification teaches SEQ ID NOS: 42 and 43 were identified by data mining of sequences in the Incyte Genomics LIFESEQ database using CLASP software (see pages 118-119). Applicants allege that SEQ ID NOS: 42 and 43 are considered to have a "CLASP 5" profile, wherein "to qualify as a CLASP 5 candidate, a gene must be differentially expressed in tumor libraries in the tissue of interest compared to normal libraries for all tissues" (see page 119, lines 23-25). The specification is silent with respect to any potential nucleic acids that fall within Claim 1(c) or (d) or Claims 21-25.

The data provided for SEQ ID NOS: 42 and 43 is the following:

DEX0293_42	Prostate	5H
DEX0293_43	Prostate	5H

The relative expression levels were as follows:

DEX0293_42 SEQ ID NO: 42 THR.0045 PAN .0059 OVR 0.123 MAM .0255

DEX0293_43 SEQ ID NO: 43 THR.0045 PAN .0059 OVR 0.123 MAM .0255

Abbreviations for tissues:

THR Thyroid Gland; OVR Ovary; MAM Breast; PAN (no tissue is named, but it appears as if it is to be from the Pancreas).

(This data is found on page 119, lines 27-29, and page 120, lines 5-6 and 11-16)

Additionally, it is noted the specification is silent as to any data for the nucleic acids encompassed within Claim 1(c) or (d) or Claims 21-25.

Evaluating the data above, several aspects of Applicants' assertions are unclear. First, referring to the table above, it is not clear as to what "5H" stands for, whether "Prostate" means the sample was taken from a diseased or a healthy patient, whether diseased and normal samples were expressed and then compared against one another, how many patients these results stem from, and furthermore, it is not clear as to what was the source of the nucleic acids (e.g., cell culture or tumor). Additionally, the relative expression values are also vague. These values show expression levels in samples from the thyroid gland, ovary, breast and potentially pancreas. However, it is not clear whether these samples comprise data from diseased or normal samples, a comparison of both, whether these values represent a comparison of expression of prostate and these other tissues, etc. Except for the table and relative expression levels above, the specification is silent as to any information regarding SEQ ID NOS: 42 or 43 (or nucleic acids encompassed by Claim 1(c) or (d)), and specifically, the specification is silent as to any correlation between SEQ ID NOS: 42 or 43 (or nucleic acids encompassed by Claim 1(c) or (d) or Claims 21-25) and methods for identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate.

MPEP § 2107.01 states:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities... An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

In the instant case, further research to identify or reasonably confirm a "real world" context of use would be required. For example, in order for a nucleic acid to be useful for detection, diagnosis and/or treatment of a disease, there must be a well established or disclosed correlation or relationship between the claimed nucleic acid and a disease or disorder. The presence of a nucleic acid in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed nucleic acid and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed nucleic acid to be used in a diagnostic manner. Many nucleic acids are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed nucleic acid is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed nucleic acid as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner* v. *Manson*, 148 USPQ 696 (US SupCt 1966).

Specifically, in the instant case, the specification does not provide any assay that clearly demonstrates a correlation between SEQ ID NOS: 42 or 43 (or nucleic acids encompassed by Claim 1, (c) or (d) or Claims 21-25) and methods for identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate. That

is, the specification does not teach any assay or expression analysis that indicates the relationship between SEQ ID NOS: 42 or 43 (or nucleic acids encompassed by Claim 1, (c) or (d) or Claims 21-25) and prostate cancer. At best, Applicants have proposed a starting point for further research in order to determine whether SEQ ID NOS: 42 or 43 is correlated with prostate cancer. Accordingly, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

II. *The specification is not supported by a well-established utility because one of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics on the invention.*

MPEP 2107 states:

> An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible."

Applicants have provided little to no evidence of the characteristics of the claimed nucleic acids, the asserted utility is not substantial, and based on Applicants assertion that the claimed nucleic acid is new (see page 1, lines 9-10), it is not apparent as to how "a person of ordinary skill in the art would immediately appreciate why the invention is useful". This is evidenced by the fact that further research would need to be carried out by the skilled artisan even given Applicants' claimed nucleic acids (see above). For these reasons, the specification is not supported by a well-established utility.

Accordingly, the claimed invention lacks a substantial and well-established utility.

Claim Rejections - 35 USC § 112

6. Claims 1-5, 7-9, 15 and 18-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility

or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, in addition to the reasons above, the specification is further not enabling because the specification does not establish that in the general population SEQ ID NOS: 42 and 43 are overexpressed in prostate tumor versus other tumor cells or versus normal cells.

MPEP 2164.01 states:

> Even though the statute does not use the term 'undue experimentation,' it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation. These factors include, but are not limited to:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

(1) ***Nature of the Invention & Breadth of the Claims***

The claims are drawn to isolated nucleic acid molecules comprising a nucleic acid sequence encoding SEQ ID NO: 96, SEQ ID NOS: 42 or 43, nucleic acid molecules that selectively hybridizes under stringent conditions to a nucleic acid that encodes SEQ ID NO: 96 or SEQ ID NOS: 42 or 43, and nucleic acids having at least 90% sequence identity over its entire

length to a nucleic acid sequence encoding SEQ ID NO: 96 or SEQ ID NOS: 42 or 43, wherein said nucleic acid molecules are differentially expressed in prostate cancer tissue.

Thus, the claims are drawn to a large genus of possible nucleic acids, including sequences from other species, mutated sequences, and allelic variants having different functional activities than that of the nucleic acids of SEQ ID NOS: 42 or 43, and nucleic acids encoding the polypeptide of SEQ ID NO: 96.

(2) ***Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The specification teaches SEQ ID NOS: 42 and 43 were identified by mRNA subtraction analysis (see pages 116-117). Additionally, the specification teaches the data provided above in the 35 U.S.C. 101 rejection, which is incorporated herein. However, the specification does not provide any working examples of using the claimed nucleic acids for identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate. Additionally, the specification does not provide any evidence the claimed nucleic acids can be in fact be used in identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate.

Furthermore, the specification does not teach several elements that would be necessary to enable the skilled artisan to use the nucleic acids of the invention. First, it is not clear as to what the source of the library is (e.g., primary tumor tissue versus a cell line) from which the claimed nucleic acids were obtained from. This is an important inquiry, since gene expression in primary tumor cells is often distinct from that which occurs in cell lines (see Dermer et al. Bio/Technology (1994) 12: 320). Assuming Applicants procured the claimed nucleic acids from

a primary tumor, the specification does not teach how many samples are present in the library. If Applicants derived expression results from a library containing only one sample, any expression data would not be applicable to the general population. That is, data from one individual is not representative of data that will or may occur in other diseased or normal patients. Thus, even assuming the specification teaches the claimed nucleic acids are overexpressed in prostate tumor cells obtained from a single source, the specification has not established that in the general population that the claimed nucleic acids are overexpressed in prostate tumor versus normal cells. Additionally, the specification does not teach a comparative readout of expression among prostate tissue (if tested) versus expression of the claimed nucleic acids in other tissues. The data summarized above does not conclusively teach such comparative expression analysis, showing overexpression in prostate tumor cells versus other tumor cell types (e.g., from ovary, breast, etc.) or normal tissue cells (e.g., from prostate, ovary, breast, etc.). Furthermore, the specification does not teach what sequences were being compared in the CLASP analysis, what tissues were involved, what types of individuals were screened, and what activity or function the polypeptide of SEQ ID NO: 96 has.

With respect to Claim 1(c) and (d) and Claims 21-25, the claims are drawn to a plurality of possible nucleotide sequence variants of SEQ ID NOS: 42 or 43, wherein the specification does not provide any guidance as to alter nucleic acid sequences falling within Claim 1(c) and (d) Claims 21-25, nor does it teach how to use said sequences. Specifically, the specification is silent as to any variants of SEQ ID NOS: 42 or 43.

Accordingly, the relative skill in the art is high, there are no working examples provided for using the claimed nucleic acids, and the specification has provided little to no guidance for using the claimed nucleic acids.

(3) ***Quantity of Experimentation Necessary & the Unpredictability of the Art***

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art.

In the instant case, the specification, nor the prior art teach an association/and or correlation for SEQ ID NOS: 42 or 43 (or nucleic acids encompassed by Claim 1(c) or (d) and Claims 21-25), and therefore, the skilled artisan would not know how to use the claimed nucleic acids. Any potential results that the skilled artisan would arrive at would be unpredictable given the lack of guidance in the specification and the prior art (see above). For example, the specification teaches that the tumor of interest (i.e., prostate tumor library) was compared to normal libraries for all tissues (see page 119, lines 24-25). However, it is not clear as to whether all the normal tissues were combined, since there is only expression data for 4 tissues, wherein normal prostate expression data is not included (see page 120, lines 5-6). Therefore, assuming that SEQ ID NOS: 42 and 43 are overexpressed, and the specification only teaches the expression of combined normal tissues (versus normal prostate tissue expression), the skilled

artisan would not know how to practice the invention because it is not clear as to what level of expression is associated with cancer. Additionally, given the lack of guidance in the specification or the prior art, as to how to alter the claimed nucleotide molecules and retain the activity of SEQ ID NO: 96, the making and using of the nucleic acid molecules encompassed by the claimed invention would also be unpredictable. Finally, the suitability of cell lines, as general models for primary tumors are also unpredictable. For example, Dermer (cited above) teaches:

> [w]hen a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary type step that enables the new cell line to thrive in its artificial environment...Yet normal or malignant cells in vivo are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of the lab dish and in the body has been in the scientific literature for more than 30 years, evidence that has been systematically ignored by the cancer establishment.

(1st column, page 320).

Therefore, if the nucleic acids in Example 1 were procured from cell lines, then extrapolating expression data from SEQ ID NOS: 42 and 43 for identifying, diagnosing, monitoring, staging, imaging and treating prostate cancer and non-cancerous disease states in prostate would be highly unpredictable.

In order to carry out making and using of the claimed nucleic acids, the experimentation required by the skilled artisan would be considered undue. First, the skilled artisan would have to experiment by altering any of the plurality of possible sequences encompassed by the claims to determine what sequences can be altered, and how they can be altered, and still retain the function of SEQ ID NO: 96. Additionally, once the sequences were obtained, the skilled artisan would have to carry out expression analysis studies on many samples from different tissues from

both normal and diseased test subjects (including normal and malignant prostate tissues from cell culture and patients' samples, as well as, in cells from unrelated tissues). Following this experimentation, the skilled artisan would have to determine whether the sequences are specific for a disease state. Significance of any increased expression levels needs to be established; as there are usually variations in tissues obtained from different individuals, therefore studies involving statistically significant numbers of patients would also need to be performed. Such experimentation requires a large amount of trial and error analysis, with little to no starting point, absent any teaching in the specification (see above), wherein the results of such analysis are unpredictable, and is therefore considered undue.

In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. However, "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". (*Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001).

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Applicants Arguments

Applicants argue that it is clear that SEQ ID NOS: 42-43 were differentially expressed in prostate cancer tissue libraries, as compared to normal libraries, and this differential expression constitutes a "pharmacological activity relevant to the asserted use as a diagnostic for prostate cancer, thus satisfying the utility requirement." See page 21 of Applicants response. Applicants also argue the specification teaches detailed teachings of nucleic acid molecules meeting the

limitations of Claim 1(c) and (d) on pages 31-40, and that "MPEP § 2107.03 and the courts are quite clear, evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility is routinely supportive of an assertion of therapeutic utility for the structurally similar compound." See page 21 of Applicants response. Applicants also reiterate some of the issues raised in the rejection, such as "what 5H stands for in the data table at page 119-120," and "how many patients these results stem from, and what the source of the nucleic acids is (e.g., cell culture of tumor)." See page 19 of Applicants response.

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, it is not clear as to what is meant or encompassed by "differentially expressed in prostate cancer tissue," and therefore, it is not clear what expression levels were actually obtained, if any, in samples from prostate cancer tissue libraries or normal prostate tissue libraries. (See 112, 2nd paragraph above) Next, Applicants did not show either that the nucleic acids encompassed by the claims are expressed only in prostate cancer tissue or that they have any pharmacological activity. Applicants have not provided any comparative data for the level of expression of the claimed nucleic acids in cancerous vs. normal tissue, which is critical to the utility of claimed nucleic acids as being indicative of tumorigenesis. In addition, despite Applicants' assertions, pages 31-40 do not provide any specific nucleic acid sequences (or variants) of the nucleic acids encompassed by Claim 1(c) or (d) or Claims 21-25. Furthermore, even assuming Applicants did provide these nucleic acid sequences, SEQ ID NOS: 42 and 43 do not have a "particular therapeutic or pharmacological utility," and therefore, the nucleic acids of Claims 1(c) and (d) and Claims do not meet the utility requirements. Finally, while Applicants

reiterate issues raised in the rejection (e.g., "what 5H stands for in the data table at page 119-120," "how many patients these results stem from," and "what the source of the nucleic acids is, e.g., cell culture of tumor,") Applicants do not provide explanations to these issues. Accordingly, the rejection is maintained.

Written Description

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 7-9, 15 and 18-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are directed to isolated nucleic acid molecules comprising a nucleic acid sequence that selectively hybridizes under stringent conditions to a nucleic acid that encodes SEQ ID NO: 96 or SEQ ID NOS: 42 or 43, and nucleic acids having at least 90% sequence identity over its entire length to a nucleic acid sequence encoding SEQ ID NO: 96 or SEQ ID NOS: 42 or 43, wherein said nucleic acid molecules are differentially expressed in prostate cancer tissue. These nucleic acids are inclusive of sequences from other species, mutated sequences, allelic variants, full-length genes, genomic DNA, etc., all which have different functions than that of the nucleic acid encoding SEQ ID NO: 96. Accordingly, the claims

include a large genus of nucleic acids encoding polypeptides, having unique functional activities, whereas applicants only disclose two members of the genus (i.e., SEQ ID NOS: 42 and 43).

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only two members (SEQ ID NOS: 42 and 43) have been defined by its structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., restriction map, chromosomal map position, biological activity of an encoded protein, promoters, enhancers, 5' or 3' untranslated regions, etc.). In the instant case, no such identifying characteristics have been provided for ant of the nucleic acids.

In *The Reagents of the University of California v. Eli Lilly and Co.,* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention". In the instant case, the claims are drawn to generic statements, which define a genus of nucleic acids by only their alleged functional activity; however, the specification does not provide an adequate written description of this genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." (emphasis added)

While at the time filing Applicants were in possession of SEQ ID NOS: 42 and 43, the specification does not support the broadly claimed genus. Accordingly, the claimed invention lacks an adequate written description.

Applicant's attention is also drawn to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1st Paragraph, Written Description Requirement" (published in Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111).

Applicants Arguments

Applicants argue amended Claim 1, which was amended to "clarify that the nucleic acid molecule is prostate cancer specific and differentially expressed in prostate cancer tissue," and therefore, "the nucleic acid molecules have a similar function." See page 23 of Applicants' response. Applicants also argue pages 13-16 and Example 1 teaches methods for ascertaining sequences that meet the structural and functional limitations of the instant amended claims. See page 23 of Applicants' response. Furthermore Applicants argue "upon discovery of the instant claimed nucleic acid sequence of SEQ ID NO: 42 or 43 and their differential expression in prostate tumor tissues, Applicants were clearly in possession of additional nucleic acid sequences identified in accordance with routine procedures based upon these reference sequences." See page 24 of Applicants' response.

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, it is not clear what is meant by "prostate specific" and "differentially expressed in prostate cancer tissue," and therefore, it is not clear what functional limitation this adds to the Claim 1 (see 112, 2nd paragraph rejection above). Next, while pages 13-16 and Example 1 teaches general concepts relating to sequence identity, sequence similarity and hybridization parameters, these passages do not demonstrate that Applicants were in *possession* of the genus of nucleic acids encompassed by the claims. Furthermore, the assertion that a skilled artisan performs some methods routinely does not mean that Applicants were in possession of the claimed nucleic acids. Except for the description of SEQ ID NOS: 42-43, Applicants have not provided an adequate written description to support the broadly claimed genus of nucleic acids. Finally, it is not clear how the disclosure of SEQ ID NOS: 42-43 and its alleged expression in prostate cancer tissues, demonstrates that Applicants were "clearly" in possession of additional nucleic acids. There is no evidence in the record to support Applicants assertions that given the disclosure of SEQ ID NOS: 42-43, Applicants were "clearly" in possession of additional nucleic acids encompassed by the claims. Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-5, 7-9 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Shimkets et al. (WO 00/58473).

Shimkets teaches a nucleic acid (SEQ ID NO: 4273) which comprises a nucleic acid molecule that selectively hybridizes under stringent conditions to a nucleic acid that encodes SEQ ID NO: 96 or SEQ ID NOS: 42 or 43 (see pages 3477-3479, N_Geneseq Accession No. AAC76582 in sequence search result #3, and N_Geneseq Accession No. AAC76582 in sequence search result #9). Accordingly, Shimkets anticipates Claim 1.

With respect to Claims 2-3, Shimkets teaches the nucleic acid is cDNA or genomic DNA (page 13, lines 6-7).

With respect to Claims 4-5, Shimkets teaches the nucleic acid is a mammalian (e.g., human) nucleic acid molecule (pages 3477-3479).

With respect to Claims 7-9, Shimkets teaches vectors, host cells and methods of producing a polypeptide (see page 1, lines 20-23; page 2, lines 13-18, pages 38-43)

With respect to Claim 15, Shimkets teaches a kit comprising means for determining the presence of the claimed nucleic acids (see page 5504).

11. Claims 1-5, 7-9 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Faris et al. (US Pub. No. US2002/0150972)

Faris teaches a nucleic acid (SEQ ID NO: 1) which comprises a nucleic acid molecule that selectively hybridizes under stringent conditions to a nucleic acid that encodes SEQ ID NO: 96 or SEQ ID NOS: 42 or 43 (see pages 41-43 and Published Applications sequence search result #3). Accordingly, Faris anticipates Claim 1.

With respect to Claims 2-3, Faris teaches the nucleic acid is cDNA or genomic DNA (see page 8, paragraph 0082).

With respect to Claims 4-5, Faris teaches the nucleic acid is a mammalian (e.g., human) nucleic acid molecule (see page 1, paragraph 0009, Example 1 and page 41).

With respect to Claims 7-9, Faris teaches vectors, host cells and methods of producing a polypeptide (see page 9 and page 149, 2nd column)

With respect to Claim 15, Faris teaches a kit comprising means for determining the presence of the claimed nucleic acids (see page 24, 2nd column to page 25, 1st column).

Applicants Arguments

Applicants argue the amendments to Claim 1 obviate the rejections of Shimkets and Faris.

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive. It is noted the 102 rejections apply to only Claim 1(c). The nucleic acids taught by Shimkets and Faris will selectively hybridizes under stringent conditions to a nucleic acid that encodes SEQ ID NO: 96 or SEQ ID NOS: 42 or 43, and therefore, the teachings of Shimkets and Faris anticipate the claimed invention.

Conclusion

12. No claims are allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (571) 272-0747. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler
July 28, 2004

CARLA J. MYERS
PRIMARY EXAMINER